

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C.20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 16 March 2000 (16.03.00)	
International application No. PCT/IL99/00079	Applicant's or agent's file reference 116745.1 RS
International filing date (day/month/year) 05 February 1999 (05.02.99)	Priority date (day/month/year) 07 August 1998 (07.08.98)
Applicant BAR-SHAVIT, Rachel	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
20 February 2000 (20.02.00)

☐ in a notice effecting later election filed with the International Bureau on:  
\_\_\_\_\_

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Olivia RANAIVOJAONA

Telephone No.: (41-22) 338.83.38

PCT  
PTO/PCT Rec'd 2/8 JAN 2001  
REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference  
(if desired) (12 characters maximum) 116745.1 RS

Box No. I TITLE OF INVENTION  
METHOD FOR TREATMENT OF INVASIVE CELLS

Box No. II APPLICANT

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)  
HADASIT MEDICAL RESEARCH SERVICES &  
DEVELOPMENT COMPANY LTD.  
P.O.Box 12000  
Kiryat Hadassah  
Jerusalem 91120  
Israel

☐ This person is also inventor.

Telephone No.

Facsimile No.

Teleprinter No.

State (that is, country) of nationality:  
IL

State (that is, country) of residence:  
IL

This person is applicant for the purposes of: ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)  
BAR-SHAVIT, Rachel  
44 Peretz Berenstein Street  
Ramat-Shanet  
Jerusalem 96920  
Israel

This person is:

☐ applicant only

☒ applicant and inventor

☐ inventor only (if this check-box is marked, do not fill in below.)

State (that is, country) of nationality:  
IL

State (that is, country) of residence:  
IL

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE, OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:

☒ agent ☐ common representative

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)  
REINHOLD COHN AND PARTNERS  
P.O.Box 4060  
Tel-Aviv 61040  
Israel

Telephone No.

+972 3 7109312/3

Facsimile No.

+972 3 5806405

Teleprinter No.

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

LegalForm 1999, Form PCTREQ

See Notes to the request form

Form PCT/RO/101 (first sheet) (July 1998)

## Box No. V DESIGN OF STATES

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

## Regional Patent

- ☐ AP ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SZ Swaziland, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☐ EA Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ EP European Patent: AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☐ OA OAPI Patent: BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line) .....

## National Patent (if other kind of protection or treatment desired, specify on dotted line):

- |   |   |
|---|---|
| <input type="checkbox"/> AL Albania .....                               | <input type="checkbox"/> LS Lesotho .....                                   |
| <input type="checkbox"/> AM Armenia .....                               | <input type="checkbox"/> LT Lithuania .....                                 |
| <input type="checkbox"/> AT Austria .....                               | <input type="checkbox"/> LU Luxembourg .....                                |
| <input type="checkbox"/> AU Australia .....                             | <input type="checkbox"/> LV Latvia .....                                    |
| <input type="checkbox"/> AZ Azerbaijan .....                            | <input type="checkbox"/> MD Republic of Moldova .....                       |
| <input type="checkbox"/> BA Bosnia and Herzegovina .....                | <input type="checkbox"/> MG Madagascar .....                                |
| <input type="checkbox"/> BB Barbados .....                              | <input type="checkbox"/> MK The former Yugoslav Republic of Macedonia ..... |
| <input type="checkbox"/> BG Bulgaria .....                              |   |
| <input type="checkbox"/> BR Brazil .....                                | <input type="checkbox"/> MN Mongolia .....                                  |
| <input type="checkbox"/> BY Belarus .....                               | <input type="checkbox"/> MW Malawi .....                                    |
| <input checked="" type="checkbox"/> CA Canada .....                     | <input type="checkbox"/> MX Mexico .....                                    |
| <input type="checkbox"/> CH and LI Switzerland and Liechtenstein .....  | <input type="checkbox"/> NO Norway .....                                    |
| <input type="checkbox"/> CN China .....                                 | <input type="checkbox"/> NZ New Zealand .....                               |
| <input type="checkbox"/> CU Cuba .....                                  | <input type="checkbox"/> PL Poland .....                                    |
| <input type="checkbox"/> CZ Czech Republic .....                        | <input type="checkbox"/> PT Portugal .....                                  |
| <input type="checkbox"/> DE Germany .....                               | <input type="checkbox"/> RO Romania .....                                   |
| <input type="checkbox"/> DK Denmark .....                               | <input checked="" type="checkbox"/> RU Russian Federation .....             |
| <input type="checkbox"/> EE Estonia .....                               | <input type="checkbox"/> SD Sudan .....                                     |
| <input type="checkbox"/> ES Spain .....                                 | <input type="checkbox"/> SE Sweden .....                                    |
| <input type="checkbox"/> FI Finland .....                               | <input type="checkbox"/> SG Singapore .....                                 |
| <input type="checkbox"/> GB United Kingdom .....                        | <input type="checkbox"/> SI Slovenia .....                                  |
| <input type="checkbox"/> GE Georgia .....                               | <input type="checkbox"/> SK Slovakia .....                                  |
| <input type="checkbox"/> GH Ghana .....                                 | <input type="checkbox"/> SL Sierra Leone .....                              |
| <input type="checkbox"/> GM Gambia .....                                | <input type="checkbox"/> TJ Tajikistan .....                                |
| <input type="checkbox"/> GW Guinea-Bissau .....                         | <input type="checkbox"/> TM Turkmenistan .....                              |
| <input type="checkbox"/> HR Croatia .....                               | <input type="checkbox"/> TR Turkey .....                                    |
| <input type="checkbox"/> HU Hungary .....                               | <input type="checkbox"/> TT Trinidad and Tobago .....                       |
| <input type="checkbox"/> ID Indonesia .....                             | <input type="checkbox"/> UA Ukraine .....                                   |
| <input type="checkbox"/> IL Israel .....                                | <input type="checkbox"/> UG Uganda .....                                    |
| <input type="checkbox"/> IS Iceland .....                               | <input checked="" type="checkbox"/> US United States of America .....       |
| <input checked="" type="checkbox"/> JP Japan .....                      |   |
| <input type="checkbox"/> KE Kenya .....                                 | <input type="checkbox"/> UZ Uzbekistan .....                                |
| <input type="checkbox"/> KG Kyrgyzstan .....                            | <input type="checkbox"/> VN Viet Nam .....                                  |
| <input type="checkbox"/> KP Democratic People's Republic of Korea ..... | <input type="checkbox"/> YU Yugoslavia .....                                |
|   | <input type="checkbox"/> ZW Zimbabwe .....                                  |
| <input type="checkbox"/> KR Republic of Korea .....                     |   |
| <input type="checkbox"/> KZ Kazakhstan .....                            |   |
| <input type="checkbox"/> LC Saint Lucia .....                           |   |
| <input type="checkbox"/> LK Sri Lanka .....                             |   |
| <input type="checkbox"/> LR Liberia .....                               |   |

Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after issuance of this sheet:

**Precautionary Designation Statement:** In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)

Box No. VI PRIORITY CLAIM		<input type="checkbox"/> Further priority claims are indicated in the Supplemental Box.		
Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:		
		national application: country	regional application: regional Office	international application: receiving Office
item (1) 7 August 1998 (04.08.1998)	125698	IL		
item (2)				
item (3)				

☒ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office) identified above as item(s): (1)

\* Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(h)(ii)). See Supplemental Box.

## Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA)  
(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):

ISA/US

Request to use results of earlier search; reference to that search (if an earlier search has been carried out by or requested from the International Searching Authority):

Date (day/month/year) Number Country (or regional Office)

## Box No. VIII CHECK LIST: LANGUAGE OF FILING

This international application contains the following number of sheets:

request : 3  
description (excluding sequence listing part) : 17  
claims : 2  
abstract : 1  
drawings : 11  
sequence listing part of description :  
Total number of sheets : 34

This international application is accompanied by the item(s) marked below:

1. ☒ fee calculation sheet
2. ☐ separate signed power of attorney
3. ☐ copy of general power of attorney; reference number, if any:
4. ☐ statement explaining lack of signature
5. ☐ priority document(s) identified in Box No. VI as item(s):
6. ☐ translation of international application into (language):
7. ☐ separate indications concerning deposited microorganism or other biological material
8. ☐ nucleotide and/or amino acid sequence listing in computer readable form
9. ☐ other (specify):

Figure of the drawings which should accompany the abstract:


Fig.2

Language of filing of the international application:

ENGLISH

## Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).



PATINKIN Jonathan  
Agent for REINHOLD COHN AND PARTNERS

For receiving Office use only		2. Drawings: <input type="checkbox"/> received: <input type="checkbox"/> not received:
1. Date of actual receipt of the purported international application:		
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:		
4. Date of timely receipt of the required corrections under PCT Article 11(2):		
5. International Searching Authority (if two or more are competent): ISA/	6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid	

For International Bureau use only	
Date of receipt of the record copy by the International Bureau:	

Form PCT/RO/101 (last sheet) (July 1998)

LogoStar 1998, Form PCTREQ See Notes to the request form

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

3  
REC'D 23 MAY 2000

WIPO

PCT

Applicant's or agent's file reference 116745.1LK	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/IL99/00079	International filing date (day/month/year) 05 FEBRUARY 1999	Priority date (day/month/year) 07 AUGUST 1998
International Patent Classification (IPC) or national classification and IPC IPC(7): C12N 15/12; A61K 37/02 and US Cl.: 536/23.5; 435/69.1, 325, 320.1; 514/13		
Applicant HADASIT MEDICAL RESEARCH SERVICES & DEVELOPMENT COMPANY LTD.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 3 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand  20 FEBRUARY 2000	Date of completion of this report  20 APRIL 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer  JAMES H. REAMER Telephone No. (703) 308-1235

JOYCE BRIDGERS  
PARALEGAL SPECIALIST  
CHEMICAL MATRIX

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/IL99/00079

## I. Basis of the report

1. With regard to the **elements** of the international application:\*

☒ the international application as originally filed

☒ the description:

pages 1-17, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_

☒ the claims:

pages 18-19, as originally filed  
pages NONE, as amended (together with any statement) under Article 19  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_

☒ the drawings:

pages 1-25, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_

☒ the sequence listing part of the description:

pages 1-15, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.  
These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.  
☐ filed together with the international application in computer readable form.  
☒ furnished subsequently to this Authority in written form.  
☒ furnished subsequently to this Authority in computer readable form.  
☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

- ☒ the description, pages NONE  
☒ the claims, Nos. NONE  
☒ the drawings, sheets/fig NONE

5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\*Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/IL99/00079

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

### 1. statement

Novelty (N)

Claims 1-19 YES

Claims NONE NO

Inventive Step (IS)

Claims 1-19 YES

Claims NONE NO

Industrial Applicability (IA)

Claims 1-19 YES

Claims NONE NO

### 2. citations and explanations (Rule 70.7)

Claims 1-19 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the use of treatment of metastatic tumor cells with an antisense molecule comprising a nucleotide sequence which is complementary to an RNA sequence of a protease activated receptor protein. These antisense molecules have industrial applications in the treatment of cancers and for treating disorders involving the implantation of a placenta in a female subject.

----- NEW CITATIONS -----  
NONE